Severe Photosensitivity Causing Multifocal Squamous Cell Carcinomas Secondary to Prolonged Voriconazole Therapy

Kate L. McCarthy,1 E. Geoffrey Playford,2 David F. M. Looke,2 and Michael Whitby2

1Sullivan and Nicolaides Pathology and 2Infection Management Services, Princess Alexandra Hospital, Queensland, Australia

A 32-year-old woman was treated with long-term voriconazole therapy for recurrent aspergillosis associated with chronic granulomatous disease. A short time after commencement of voriconazole therapy, a severe photosensitivity reaction developed. Continued voriconazole exposure led to the development of multifocal facial squamous cell carcinomas. The photosensitivity reaction resolved after the patient changed therapy to posaconazole.

Discussion. Voriconazole, a broad-spectrumazole antifungal agent, has been associated with dermatological complications, mostly mild skin rashes. Severe reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been occasionally reported [2–4]. Photosensitivity reactions, such as erythema, cheilitis, hyperpigmentation of the hands, exfoliative dermatitis, discoid erythematous lesions, pseudo-
porphyria, and discoid lupus vulgaris, have also been infrequently reported [5–10, 13–15]. Although solar elastic changes, multiple lentigines, and ephelides in sun-exposed areas have complicated photosensitivity reactions from prolonged voriconazole exposure [10, 11], no cases of multifocal and highly invasive SCCs complicating voriconazole-induced photosensitivity reactions have been documented.

Of the other Aspergillus-active azole agents, only itraconazole has also been associated with a photosensitivity dermatitis [16] but not with the development of skin malignancies. The mechanism of voriconazole-induced photosensitivity remains uncertain, but the photosensitivity reactions may be a direct effect of voriconazole therapy or one of its metabolites or, alternatively, an indirect retinoid effect of voriconazole therapy [5, 6, 10, 11]. Such photosensitivity reactions appear to be idiosyncratic, rather than dependent on dose [3]. Long-term voriconazole therapy has not previously been reported to be associated with skin malignancy [17, 18]. For our patient, the long-term voriconazole exposure and, consequentially, the prolonged photosensitivity reaction in the context of high, year-round ultraviolet exposure were likely important predispositions to the development of the SCCs. Although the underlying chronic granulomatous disease may have, in part, predisposed the patient to the photosensitivity reaction [11–14], no association with SCCs has been reported.

In summary, we highlight that, when complicated by a photosensitivity reaction, prolonged voriconazole therapy, particularly in the context of significant ultraviolet exposure, causes risk of the development of multifocal invasive SCCs. Therefore, in such contexts, an alternate agent should be used whenever possible.

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References